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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/070,775	03/07/2002	Mohamend El-Sherbeini		9605

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EXAMINER

DEVI, SARVAMANGALA J N

ART UNIT	PAPER NUMBER
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1645

DATE MAILED: 04/02/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

84.

Office Action Summary

Application No.

10/070,775

Applicant(s)

EL-SHERBEINI ET AL.

Examiner

S. Devi, Ph.D.

Art Unit

1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 22 December 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-11 and 15-17 ~~is/are~~ are pending in the application.
- 4a) Of the above claim(s) 7-11 and 15-17 ~~is/are~~ are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-6 ~~is/are~~ are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input checked="" type="checkbox"/> Other: <u>Sequence alignment report</u> . |

DETAILED ACTION

Preliminary Amendments

- 1) Acknowledgment is made of Applicants' preliminary amendments filed 12/22/03, 09/29/03 and 03/07/02.

Election

- 2) Acknowledgment is made of Applicants' election filed 09/29/03 in response to the lack of unity mailed 08/29/03. Applicants have elected invention I, claims 1-6, with traverse. Applicants' traversal is on the grounds that the amended claim 1 does not refer to sequences that hybridize to a sequence that encodes the polypeptide of SEQ ID NO: 2 and therefore, Liao *et al.* is no longer applicable as reference that teaches the special technical feature. Applicants further contend that claims of invention I define the sequence, which should also be considered as the special technical feature relating to the claims of inventions I and IV.

Applicants' arguments have been carefully considered, but are non-persuasive. Claim 1, as originally filed and as amended, presents more than one Markush polynucleotide species. The prior art has to disclose only one of these polynucleotide sequence species. Liao *et al.* is still applicable since this reference taught a polynucleotide having more than 99% local sequence identity to the instantly recited SEQ ID NO: 1, which would be expected to comprise a polynucleotide that is at least partially complementary to the polynucleotide of SEQ ID NO: 1. See the rejection(s) made below. Therefore, the reasons upon which the lack of unity is based are proper.

Status of Claims

- 3) Claims 12, 13 and 14 have been canceled via the amendment filed 03/07/02.

Claims 1, 8, 9 and 15 have been amended via the amendment filed 03/07/02.

Claim 1 has amended via the amendment filed 09/29/03.

Claims 1-11 and 15-17 are pending.

Claims 7-11 and 15-17 are withdrawn from consideration as being directed to non-elected inventions. See 37 C.F.R. 1.142(b) and M.P.E.P. § 821.03.

Claims 1-6 have been elected and are under examination. A First Action on the Merits on these claims is issued.

Sequence Listing

- 4) Acknowledgment is made of Applicants' submission of the raw sequence listing and the CRF which have been entered on 01/04/04.

Priority

- 5) The instant application is a national stage 371 application of PCT/US00/24743, filed 09/11/2000, and claims priority to the provisional application, 60/154,117 filed 09/15/1999 in the United States.

Specification - Informalities

- 6) The specification is objected to for the following reasons:

(i) The use of the trademarks in the instant specification has been noted in this application. For example, page 21, line 33 and line 17 on page 16: 'Novagen'; and page 16, line 18: 'Invitrogen' and 'Pharmacia'. Although the use of trademarks is permissible in patent applications, the propriety nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks. It is suggested that Applicants examine the whole specification and make necessary changes wherever trademark recitations appear.

(ii) The specification on page 21 contains incomplete information on the allegedly deposited plasmid, pPaeMurE.

(iii) Line 12 on page 6 of the specification ends improperly with two periods.

Rejection(s) under 35 U.S.C. § 112, First Paragraph

- 7) Claim 2 is rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

It is noted that the polynucleotide containing modified nucleotides as recited in the instant claim does not exist independent of its function, i.e., ability to encode a functional polypeptide having the amino acid sequence of SEQ ID NO: 2. The specification discloses therapeutic applications for the recited polypeptide encoded by the claimed polynucleotide. However, the instant specification fails to teach a single polynucleotide having 'modified nucleotides' (i.e., a polynucleotide variant) that encodes a polypeptide having the amino acid sequence of SEQ ID NO: 2. Therapeutic applications minimally require an ability to interact specifically with a compound. The precise structure or relevant identifying characteristics of each polynucleotide variant molecule that encodes a polypeptide of SEQ ID NO: 2 that is

functional (i.e., enzymatic) can only be determined empirically by actually making every DNA variant molecule that encodes the polypeptide, and testing each varied DNA molecule to determine whether it encodes the recited polypeptide is functional as a therapeutic agent. The *Written Description Guidelines* state:

There is an inverse correlation between the level of predictability in the art and the amount of disclosure necessary to satisfy the written description requirement. For example, if there is a well-established correlation between the structure and function in the art, one skilled in the art will be able to reasonably predict the complete structure of the claimed invention from its function.

A mere statement that the invention includes a polynucleotide containing modified nucleotides and encoding a polypeptide of SEQ ID NO: 2 is insufficient to meet the adequate written description requirement of the claimed invention. The polypeptide of SEQ ID NO: 2 has specific biologic properties dictated by the structure of the protein and the corresponding structure of the structural gene sequence which encodes it. A convincing structure-function relationship has to exist between the structure of the gene sequence, the structure of the polypeptide encoded, and the function of the encoded polypeptide. The function cannot be predicted from the modification of the structure of the gene and in the instant case, the DNA comprising the modified nucleotides and encoding the recited polypeptide of SEQ ID NO: 2. Applicants have not shown that variation or modification of a reference sequence encoding a reference polypeptide as claimed would automatically predict the production of a functional polypeptide having the desired biologic activity. The specification fails to teach the structure or relevant identifying characteristics of a representative number of species of modified DNA molecules encoding the polypeptide as recited, sufficient to allow one skilled in the art to determine that the inventors had possession of the invention as claimed. With the exception of a polynucleotide encoding the polypeptide of SEQ ID NO: 2, a skilled artisan cannot envision the detailed chemical structure of all the polynucleotide variant species encompassed by the recited molecule. Regardless of the complexity or simplicity of the method of isolation, conception cannot be achieved until reduction to practice has occurred. Adequate written description requires more than a mere statement that it is a part of the invention and a reference to a potential method of isolating it. The nucleic acid comprising the modified nucleotides itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

Rejection(s) under 35 U.S.C § 112, Second Paragraph

- 8) The following is a quotation of the second paragraph of 35 U.S.C. § 112:

The specification shall conclude one or more claims particularly pointing out and distinctly claiming the

subject matter which the Applicant regards as his/her invention.

9) Claims 1-6 are rejected under 35 U.S.C. § 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant(s) regards as the invention.

(a) Claim 5 lacks proper antecedent basis in the recitation 'a polynucleotide of claim 1'. For proper antecedence, it is suggested that Applicants replace the recitation with --the polynucleotide of claim 1--.

(b) Claim 1(b) is vague and indefinite in the recitation: 'complementary to the polynucleotide (a)', because it is unclear whether the complementary polynucleotide is partially complementary or fully complementary to the polynucleotide of (a).

(c) Claim 2 is vague, indefinite and confusing in the recitation: 'modified nucleotides', because it is unclear what is encompassed in this limitation. What constitutes modified nucleotides, and how much of the nucleotide's original structure has to be retained such that the resulting nucleotide can be considered as a 'modified nucleotide', is not clear. Does the claimed polynucleotide comprising 'modified' nucleotides encode a polypeptide having the amino acid sequence of SEQ ID NO: 2? Are the modified nucleotides comprised within that part of the claimed polynucleotide which encodes the polypeptide of SEQ ID NO: 2, or outside the coding region? The metes and bounds of the structure encompassed in the polynucleotide associated with the above-identified limitation is indeterminate.

(d) Claim 1 is vague in the recitation 'A purified and isolated polynucleotide'. Since purification takes place after isolation, it is suggested that Applicants replace the phrase with --An isolated and purified polynucleotide--.

(e) For clarity and/or proper antecedence, it is suggested that Applicants replace the limitation in claim 1(a): 'having an amino acid of SEQ ID NO: 2' with --having the amino acid sequence of SEQ ID NO: 2--.

(f) Claims 2-6, which depend directly or indirectly from claim 1, are also rejected as being indefinite, because of the vagueness or indefiniteness identified above in the base claim.

Rejection(s) under 35 U.S.C. § 102

10) The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless –

(e) the invention was described in-

(2) a patent granted on an application for patent by another filed in the United States before the

invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

11) Claims 1-3, 5 and 6 are rejected under 35 U.S.C. § 102(e)(2) as being anticipated by Rubenfield *et al.* (US 6,551,795).

Rubenfield *et al.* disclosed an isolated and purified polynucleotide, a complement and a probe thereof, and an expression vector and a host cell comprising the same. The nucleic acid is double stranded or single stranded, and contains internucleotide linkages and nucleotides that are modified. See column 2 under 'Summary of the Invention'; column 10 under 'Definition'; column 6, last paragraph; column 7; column 8, lines 1-51; column 10, lines 46-67; column 11; column 12, lines 1-61; column 15, lines 13-22; the sections following '*Ps. aeruginosa* Nucleic Acids' in columns 17-26; column 42, lines 11-32; and claims. Rubenfield's nucleic acid has more than 97% sequence identity with the instantly claimed nucleotide sequence of SEQ ID NO: 1 (see attached sequence alignment report). That the prior art polynucleotide with such high sequence identity is complementary to the instantly claimed polynucleotide of SEQ ID NO: 1 is inherent from the teachings of the prior art. That the prior art polynucleotide having more than 97% sequence identity with the claimed nucleotide sequence contains modified nucleotides is also inherent from the teachings of the prior art in light of the about 3% sequence dissimilarity.

Claims 1-3, 5 and 6 are anticipated by Rubenfield *et al.*

Relevant Prior Art

12) The prior art made of record and not currently relied upon in any of the rejections is considered pertinent to Applicants' disclosure:

- Liao *et al.* (*Antimicrob. Agents Chemother.* 39: 1871-1874, 1995) taught an isolated polynucleotide comprising a nucleotide sequence that shows more than 99% local sequence identity with the instantly claimed polynucleotide of SEQ ID NO: 1, an expression vector and a host cell comprising the same (see entire document).
- de Lencastre *et al.* (US 6,251,647 B1) disclosed an isolated polynucleotide that shows 100% local sequence identity with the instantly claimed polynucleotide of SEQ ID NO: 1. See entire document.

Remarks

13) Claims 1-6 stand rejected.

An isolated and purified polynucleotide comprising the nucleotide sequence of SEQ ID NO: 1 is free

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of prior art currently of record.

14) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center located in Crystal Mall 1. The transmission of such papers by facsimile must conform with the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The CM1 facsimile center receives transmissions 24 hours a day and 7 days a week. The RightFax number for submission of before-final amendments is (703) 872-9306. The RightFax number for submission of after-final amendments is (703) 872-9307.

15) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (571) 272-0854. The Examiner can normally be reached on Monday to Friday from 7.45 a.m. to 4.15 p.m. except one day each bi-week, which would be disclosed on the Examiner's voice mail system. A message may be left on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Lynette Smith, can be reached on (571) 272-0864.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

March, 2004



**S. DEVI, PH.D.
PRIMARY EXAMINER**

Seq ID No. 1

RESULT 1
US-09-252-991A-7930/c
; Sequence 7930, Application US/09252991A
; Patent No. 6551795
; GENERAL INFORMATION:
; APPLICANT: Marc J. Rubenfield et al.
; TITLE OF INVENTION: NUCLEIC ACID AND AMINO ACID SEQUENCES RELATING TO PSEUDOMONAS
; TITLE OF INVENTION: AERUGINOSA FOR DIAGNOSTICS AND THERAPEUTICS
; FILE REFERENCE: 107196.136
; CURRENT APPLICATION NUMBER: US/09/252,991A
; CURRENT FILING DATE: 1999-02-18
; PRIOR APPLICATION NUMBER: US 60/074,788
; PRIOR FILING DATE: 1998-02-18
; PRIOR APPLICATION NUMBER: US 60/094,190
; PRIOR FILING DATE: 1998-07-27
; NUMBER OF SEQ ID NOS: 33142
; SEQ ID NO 7930
; LENGTH: 1611
; TYPE: DNA
; ORGANISM: Pseudomonas aeruginosa
US-09-252-991A-7930

Query Match 97.5%; Score 1461.6; DB 4; Length 1611;
Best Local Similarity 99.0%; Pred. No. 8.3e-268;
Matches 1481; Conservative 0; Mismatches 14; Indels 1; Gaps 1;
QY 5 CTATGAGCTGAGCCAACTGTTCCCGAGCCGAGCGCGATCTGCTGATCCGCGAGCTGA 64
DB 1611 CTATGAGCTGAGCCAACTGTTCCCGAGCCGAGCGCGATCTGCTGATCCGCGAGCTGA 1552
QY 65 CCTGTGATAGCCACGCGTTCGTCGGTTCGACCTGTTCTTGAAGGTCGCGGCGGCACC 124
DB 1551 CCTGTGATAGCCGCGGCTTCGTCGGGCGACCTGTTCTTGGCGGTGCGGCGGCGCC 1492
QY 125 AGGATGTCGTGCGCACATCGCCGATGCCCT-GACCAAGGCGCGACTGCCGTGGCTTAC 183
DB 1491 AGGATGTCGTGCGCACATCGCCGATGCCCTGCCCAAGGCGCGGCTGCCGTGGCTTAC 1432
QY 184 GAGCGGAAGCGCGGAGAGTTGCCGCCAGCGATGCCCGCTGATCGCGTGAAGGG 243
DB 1431 GAGCGGAAGCGCGGAGAGTTGCCGCCAGCGATGCCCGCTGATCGCGTGAAGGG 1372
QY 244 CTGCGCGCAACTGTGCGCGTCCCGCGCTTTCTACGCGAGCCGAGCCCGGCTG 303
DB 1371 CTGCGCGCAACTGTGCGCGTCCCGCGCTTTCTACGCGAGCCGAGCCCGGCTG 1312
QY 304 GACCTGATCGCGTCCCGCACCAAGCGCAAGACGAGCGGTGAGCCAACTGGTGGCCAG 363
DB 1311 GACCTGATCGCGTCCCGCACCAAGCGCAAGACGAGCGGTGAGCCAACTGGTGGCCAG 1252

Db 171 TGGGAGGTGCGGATGCTTGGGCTTTCAGCCAGTTGACGGTGGCGCTGG 116

QY 364 GCCCTGGATCTGCTCGGAGCGCTGCGGCATCTGCGCACCCCTCGGCACCGGTTTCTAC 423
Db 1251 GGCCTGGATCTGCTCGGAGCGCTGCGGCATCTGCGCACCCCTCGGCACCGGTTTCTAC 1192
QY 424 GCGGCCCTGGAGAGCGGCGGCAACACGCGGACCCGCTCGGGTGCAGGCCACGCTG 483
Db 1191 GCGGCCCTGGAGAGCGGCGGCAACACGCGGACCCGCTCGGGTGCAGGCCACGCTG 1132
QY 484 GCGAGCTGAGAGCGGCGGCGGCGGCTAGGATGGAGTGTCTTCCAGCGGCTC 543
Db 1131 GCCACGCTGAAGCAGGCGCGGCGGCGGCTAGGATGGAGTGTCTTCCAGCGGCTC 1072
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QY 604 GACAGCTGACTATCAAGGTTGATGGAAGCTATGCGCGGCGCAAGGCCAAGCTGTC 663
Db 1011 GACAGCTGACTATCAAGGTTGATGGAAGCTATGCGCGGCGCAAGGCCAAGCTGTC 952
QY 664 GCTGCGCGGCTGCGGCTGCGGCTGATCAACCTGAGCAGGATTTGCGCGCTCGACTG 723
Db 951 GCTGCGCGGCTGCGGCTGCGGCTGATCAACCTGAGCAGGATTTGCGCGCTCGACTG 892
QY 724 GCGGCGAGAGCAGACTCGGAGCTGATCACTACAGCTCACGAGAGCTCGGGTTC 783
Db 891 GCGGCGAGAGCAGACTCGGAGCTGATCACTACAGCTCACGAGAGCTCGGGTTC 832
QY 784 CTCTATTGCGGAGCGGCTTCGCGCGGCTGAGCAGGCTGAGGCGGCTGCTCACTCG 843
Db 831 CTCTATTGCGGAGCGGCTTCGCGCGGCTGAGCAGGCTGAGGCGGCTGCTCACTCG 772
QY 844 CAGCGGAGGCTGCTGCGGCGGCTGCTGCGGCTTCAACCTGAGCAACCTGCTG 903
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QY 904 GCGCGGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTG 963
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QY 1024 GTGGTGTGACTACGCGCATCTCCGAGCGGCTGGAAGTCTCTGAGGCGGCTGCGT 1083
Db 591 GTGGTGTGACTACGCGCATCTCCGAGCGGCTTGAAGTCTCTGAGGCGGCTGCGT 532
QY 1084 CCGCACGCGGCGGCGGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTG 1143
Db 531 CCGCACGCGGCGGCGGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTG 472
QY 1144 AAGGTCGCTGATGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTG 1203
Db 471 AAGGTCGCTGATGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTG 412
QY 1204 GACAAACGCGCACGAGGCGGCTGCGGCGGCTCATCGCGGATATCCGCAAGGCTTGGCT 1263
Db 411 GACAAACGCGCACGAGGCGGCTGCGGCGGCTCATCGCGGATATCCGCAAGGCTTGGCT 352
QY 1264 GCGGTCGAGCAAGGTTACTTCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTG 1323
Db 351 GCGGTCGAGCAAGGTTACTTCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTG 292
QY 1324 TCCGTCGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTG 1383
Db 291 TCCGTCGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTG 232
QY 1384 ATCGACGCGTACGCGATCGGTTCTCGACATCGAGCAGGCGGCGGCGGCTGCGCGCC 1443
Db 231 ATCGACGCGTACGCGATCGGTTCTCGACATCGAGCAGGCGGCGGCGGCGGCTGCGCGCC 172
1444 TGGAGGTGCCCATGCTTGAGCCTCTTCGCGCTCAGCCAGTTGACGCTCGGCTG 1499